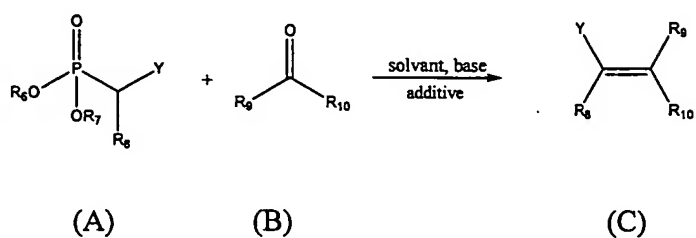


# Claims

- 1- A process for the diastereoselective preparation of olefins (C) via the Horner-Wadsworth-Emmons reaction, which consists in reacting at low temperature a phosphonate (A) with a carbonyl derivative (B) in the presence of a base, in a suitable solvent,



- in which the compounds (A) (B) and (C) are such that:

Y represents an electron-withdrawing group chosen from:

- CO<sub>2</sub>R,
- CN,
- C(O)R,
- S(O)R,
- S(O)<sub>2</sub>R,
- C(O)NRR',
- N=CRR',
- P(O)OROR',

- with R and R' as defined below,

R<sub>6</sub> and R<sub>7</sub>, taken independently, may be identical or different and represent:

- a saturated or unsaturated, linear or branched aliphatic radical containing from 1 to 24 carbon atoms, optionally substituted with hetero atoms;
- a saturated, unsaturated or aromatic, monocyclic or polycyclic cycloaliphatic radical containing from 4 to 24 carbon atoms, optionally substituted with hetero atoms;
- a saturated or unsaturated, linear or branched aliphatic radical bearing a cyclic substituent optionally substituted with hetero atoms in the aliphatic part and/or the cyclic part;

- R<sub>10</sub>, R and R', taken independently, may be identical or different and represent:

- a hydrogen atom;
- a saturated or unsaturated, linear or branched aliphatic radical containing from 1 to 24 carbon atoms, optionally substituted with hetero atoms;
- a saturated, unsaturated or aromatic, monocyclic or polycyclic cycloaliphatic radical containing from 4 to 24 carbon atoms, optionally substituted with hetero atoms;
- a saturated or unsaturated, linear or branched aliphatic radical bearing a cyclic substituent optionally substituted with hetero atoms in the aliphatic part and/or the cyclic part;

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R<sub>6</sub>, R<sub>7</sub>, R and R' may also be taken together to form a saturated, unsaturated or aromatic ring optionally comprising hetero atoms;

R<sub>8</sub> represents a radical chosen from:

- R,
  - a halogen atom,
  - OR,
  - NRR',
- with R and R' as defined above,

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R<sub>9</sub> represents a radical chosen from:

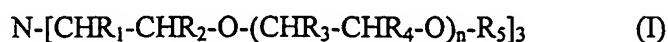
- a saturated or unsaturated, linear or branched aliphatic radical containing from 1 to 24 carbon atoms, optionally substituted with hetero atoms;
- a saturated, unsaturated or aromatic, monocyclic or polycyclic cycloaliphatic radical containing from 4 to 24 carbon atoms, optionally substituted with hetero atoms; the hetero atoms also possibly being present in the cyclic part;
- a saturated or unsaturated, linear or branched aliphatic radical bearing a cyclic substituent optionally substituted with hetero atoms in the aliphatic part and/or the cyclic part;

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with the condition that R<sub>9</sub> takes precedence over R<sub>10</sub> according to the Cahn Ingold and Prelog rules,

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characterized in that a tris(polyoxaalkyl)amine sequestering agent of formula (I):



in which:

n is an integer between 0 and 10;

R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> may be identical or different and represent a hydrogen atom or an  
5 alkyl radical containing from 1 to 4 carbon atoms;

R<sub>5</sub> represents a hydrogen atom, an alkyl or cycloalkyl radical containing up to 12  
carbon atoms, a phenyl radical or a radical of formula  $-C_mH_{2m}-\Phi$ , or  $C_mH_{2m+1}-\Phi-$ ,  
with m being an integer between 1 and 12 and  $\Phi$  being a phenyl radical;

10 is added to the reaction medium in an amount that is effective to increase the diastereo-  
selectivity of the olefins (C).

2- The process as claimed in claim 1, characterized in that the tris(polyoxaalkyl)amine  
sequestering agent is chosen from the tris(polyoxaalkyl)amines of formula (I) in  
15 which:

R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> may be identical or different and represent a hydrogen atom or a  
methyl radical;

n is an integer between 0 and 3; and

R<sub>5</sub> represents a hydrogen atom or an alkyl radical containing from 1 to 4 carbon atoms.  
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3- The process as claimed in claim 2, characterized in that the tris(polyoxaalkyl)amine  
sequestering agent is the tris(polyoxaalkyl)amine of formula (I) in which:

R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> represent a hydrogen atom;

n is 1; and

25 R<sub>5</sub> represents a methyl radical.

4- The process as claimed in any one of claims 1 to 3, characterized in that the amount  
of tris(oxaalkyl)amine sequestering agent of formula (I) used is between 0.05 and 10  
equivalents per 1 equivalent of phosphonate, one equivalent of aldehyde and one  
30 equivalent of base.

5- The process as claimed in any one of claims 1 to 4, characterized in that the amount  
of tris(oxaalkyl)amine sequestering agent of formula (I) used is 1 equivalent of tris-

(oxaalkyl)amine sequestering agent of formula (I) per 1 equivalent of phosphonate, one equivalent of aldehyde and one equivalent of base, the whole being dissolved in the solvent.

- 5 6- The process as claimed in any one of claims 1 to 5, characterized in that the phosphonate used for the reaction is chosen from the phosphonates of formula (A) in which:

Y represents  $\text{CO}_2\text{R}$ , with R representing a hydrogen atom or a linear, branched or cyclic, saturated or unsaturated alkyl radical alkyl containing from 1 to 12 carbon atoms,

- 10  $\text{R}_6$  and  $\text{R}_7$  represent a  $-\text{CH}_2\text{CF}_3$  radical, and  
 $\text{R}_8$  represents a hydrogen atom.

- 7- The process as claimed in any one of claims 1 to 6, characterized in that the phosphonate used for the reaction is chosen from the phosphonates of formula (A), in  
 15 which:

Y represents  $\text{CO}_2\text{R}$ , with R representing a methyl radical,

$\text{R}_6$  and  $\text{R}_7$  represent a  $-\text{CH}_2\text{CF}_3$  radical, and  
 $\text{R}_8$  represents a hydrogen atom.

- 20 8- The process as claimed in any one of claims 1 to 7, characterized in that the carbonyl derivative used for the reaction is preferably chosen from aldehydes, i.e.  $\text{R}_{10}$  represents a hydrogen atom.

- 9- The process as claimed in claim 8, characterized in that the aldehyde used is such that  
 25  $\text{R}_9$  is an aliphatic radical and optionally comprises ethylenic unsaturations.

10- The process as claimed in claim 9, characterized in that the radical  $\text{R}_9$  is cyclohexyl.

- 11- The process as claimed in claim 8, characterized in that the radical  $\text{R}_9$  used is  
 30 aromatic and optionally comprises one or more substitutions with alkoxy groups containing from 1 to 6 carbon atoms, or halogen atoms or  $\text{CF}_3$  groups.

12- The process as claimed in claim 11, characterized in that the radical  $R_9$  is a phenyl radical.

13- The process as claimed in any one of claims 1 to 12, characterized in that the base used is chosen from:

- amides of the type  $MNR''R'''$  with M being an alkali metal such as lithium, sodium or potassium, and  $R''$ ,  $R'''$  being chosen from alkyl radicals or radicals of alkylsilane type,
- alkoxides of the type  $MOR''$  with M being an alkali metal such as lithium, sodium or potassium, and  $R''$  being chosen from alkyl radicals,
- 10 - hydrides of the type  $MH$  with M being an alkali metal such as lithium, sodium or potassium,
- carbonates of the type  $M_2CO_3$ , with M being an alkali metal such as lithium, sodium, potassium or cesium, or an alkaline-earth metal such as calcium or barium,
- alkali metal or alkaline-earth metal hydroxides such as  $LiOH$ ,  $NaOH$ ,  $KOH$ ,  $CsOH$ ,
- 15  $Mg(OH)_2$ ,  $Ca(OH)_2$  and  $Ba(OH)_2$ , or
- organic bases, for instance 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 1,1,3,3-tetramethylguanidine (TMG) or 1,4-diazabicyclo[2.2.2]octane (DABCO) in combination with alkali metal or alkaline-earth metal halides.

14- The process as claimed in claim 13, characterized in that the base used is chosen from the potassium salt of hexamethyldisilazane (KHMDs) and potassium tert-butoxide ( $KOtBu$ ).

15- The process as claimed in any one of claims 1 to 14, characterized in that the solvent used is a polar solvent.

16- The process as claimed in claim 15, characterized in that the solvent used is chosen from ether solvents.

17- The process as claimed in claim 16, characterized in that the solvent used is chosen from tetrahydrofuran (THF) and methyl tert-butyl ether (MTBE).

18- The process as claimed in any one of claims 15 to 17, characterized in that the amount of solvent used is between 0.1 and 20 ml per mmol of phosphonate (A).

5 19- The process as claimed in any one of claims 1 to 18, characterized in that the temperature is maintained at a temperature of less than or equal to 0°C.

20- The process as claimed in any one of claims 1 to 19, characterized in that the temperature is maintained at a temperature of less than or equal to -20°C.

10 21- The process as claimed in claim 20, characterized in that the temperature is maintained at a temperature of less than or equal to -50°C.